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☐ 1. 20070232535. 27 Sep 06.
04 Oct 07. GFRalpha3 and its uses.
de Sauvage; Frederic J., et al. 435/69.1;
435/320.1 435/358 514/12 530/350
A61K39/00 20060101 C07K14/00
20060101 G01N33/53 20060101

L7: Entry 8 of 8 File: Sep 30, 1999
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DERWENT-ACC-NO: 2000-038358
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☐ 2. 20070099270. 21 Dec 06.
03 May 07. NOVEL
NEUROTROPHIC FACTORS.
Sah; Dinah W.Y., et al. 435/69.1;
435/320.1 435/358 514/12 530/350
536/23.5 A61K38/17 20060101
C07H21/04 20060101 C07K14/575
20060101 C12N5/06 20060101
C12P21/06 20060101

TITLE: New isolated GFR-alpha3 nucleic acid, used to develop products for treating diseases or conditions involving peripheral nervous system or autonomic nervous system

Basic Abstract Text (1):
NOVELTY - Isolated glial-cell-line-derived neurotrophic factor family receptor alpha-3 (GFRalpha3) polypeptides and polynucleotides are new.

☐ 3. 20060216289. 06 Jun 06.
28 Sep 06. GFRalpha3 and its uses.
de Sauvage; Frederic J., et al. 424/143.1; 435/320.1 435/325
435/69.1 435/7.1 530/350
530/388.22 536/23.5 A61K39/395
20060101 C07H21/04 20060101
C07K14/71 20060101 C07K16/28
20060101 C12P21/06 20060101
G01N33/53 20060101

Basic Abstract Text (3):
(a) NA molecule (NAM) encoding a GFRalpha3 polypeptide comprising the sequence of amino acids 27 to 400 of sequence (XV) shown (400 amino acids in length) or the sequence of amino acids 27 to 369 of sequence (XVII) (369 amino acids in length); or

☐ 4. 20050221330. 16 Jul 03.
06 Oct 05. GFRalpha3 and its uses.
de Sauvage, Frederic J., et al. 435/6;
435/320.1 435/325 435/69.1
530/350 536/23.5 C12Q001/68
C07H021/04 C07K014/71

Basic Abstract Text (10):
(a) NAM encoding a GFRalpha3 polypeptide comprising a sequence of amino acids 84 to 360 of sequence (XV), amino acids 84 to 329 of sequence (XVII), or a sequence of amino acids 110 to 386 of sequence (XX) (888 amino acids in length); or

Basic Abstract Text (15):

C12N015/09.

☐ 5. 7026138. 19 Mar 99; 11 Apr 06. Polynucleotides encoding GFR.alpha.3. de Sauvage; Frederic J., et al. 435/69.1; 435/320.1 435/325 536/23.5. C12N15/12 20060101 C12N15/79 20060101 C12N15/85 20060101 .

☐ 6. 6905817. 01 Oct 99; 14 Jun 05. Ret-independent signaling pathway for GDNF. Titievsky; Alexey Vladimirovich, et al. 435/6; 382/129 382/133 382/153 382/173 382/286 382/291 435/174 435/183 435/252.8 435/320.1 435/368 435/455 536/22.1 702/19 702/22. C12Q001/68 C12N015/00 C12N015/63 C12N001/20 C07H021/04 .

☐ 7. US 7026138 B1. New nucleic acid encoding Glial cell line-derived neurotrophic factor family receptor alpha 3 (GFRalpha3), useful for treating neurodegenerative diseases, e.g. amyotrophic lateral sclerosis, Alzheimer's disease or Parkinson's disease. DE SAUVAGE F J, et al.

☐ 8. WO 9949039 A2. New isolated GFR-alpha3 nucleic acid, used to develop products for treating diseases or conditions involving peripheral nervous system or autonomic nervous system. DE SAUVAGE F, et al.

(6) a chimeric molecule comprising a GFRalpha3 polypeptide fused to a heterologous amino acid sequence;

Basic Abstract Text (16):

(7) an antibody which specifically binds to GFRalpha3 polypeptide;

Basic Abstract Text (17):

(8) measuring agonist binding to a polypeptide comprising an agonist-binding domain of an alpha-subunit receptor, comprising exposing the polypeptide positioned in a cell membrane to a candidate agonist and measuring homo=dimerization or homo-oligomerization of the polypeptide;

Basic Abstract Text (31):

USE - The GFRalpha3 polypeptides possess neuronal cell activation function typical of the GFR protein family. GFRalpha3 ligands can be used to stimulate proliferation, growth, survival, differentiation, metabolism or regeneration of GFRalpha3- and Ret-containing cells. Agents which bind to the GFRalpha3 molecule could be useful in the treatment of diseases or conditions involving the peripheral nervous system, e.g. such ligands can be used to treat peripheral neuropathies associated with diabetes, human immunodeficiency virus (HIV), or chemotherapeutic agent treatments. Ligands binding to GFRalpha3 are expected to be useful in the treatment of neuropathic pain, antagonists of GFRalpha3 are expected to be useful to treat chronic pain of non-neuropathic nature e.g. that which is associated with various inflammatory states. GFRalpha3 or its agonist or antagonists can be used to treat conditions involving dysfunction of the autonomic nervous system including disturbances in blood pressure or cardiac rhythm, gastrointestinal function, impotence, and urinary continence. Other

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indications for ligands binding to GFRalpha3 include post-herpetic neuralgia, shingles, asthma, irritable bowel, inflammatory bowel, cystitis, headache (migraine), arthritis, spinal cord injury, constipation, hypertension, mucositis, dry mouth or eyes, fibromyalgia, chronic back pain, or wound healing. Ligands which act via GFRalpha3 will be particularly useful to treat disorders of the peripheral nervous system while inducing fewer effects on weight loss, motor function, or on kidney function than would ligands acting via GFRalpha1 or GFRalpha2. The products and methods can also be used for qualitatively and quantitatively measuring alpha-subunit receptor activation as well as facilitating identification and characterization of potential agonists and antagonists for a selected alpha-subunit receptor. The products can also be used for detection, diagnosis and production of transgenic animals.

Equivalent Abstract Text (2):

Isolation: Using sequences from the neurturin receptor GFRalpha2, a novel, potential member of the GFRalpha family was identified as a mouse expressed sequence tag (EST) in a public gene database (Acc No's W99197, AA041935, and AA050083). A DNA fragment corresponding to this potentially new receptor was obtained by PCR using mouse E15 cDNA as template and PCR primers derived from the mouse EST. The PCR product was then used to screen a lambda gt10 mouse E15 library to obtain a full length clone. A human EST database was searched and an EST (INC3574209) with 61% identity to the murine GFRalpha3 was identified. PCR amplification was then used to screen cDNA libraries. A strong PCR product was identified in all libraries analyzed (fetal lung, fetal kidney and placenta). To isolate a cDNA clone encoding this protein, a human fetal lung-PRK5 vector

library was selected and enriched for positive cDNA clones by extension of single stranded DNA from plasmid libraries grown in dug- /bung-host using a new a3.R primer. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue. Two of the isolated clones were sequenced. These cDNA sequences were designated DNA48613 and DNA48614. Amino acid sequence analysis of DNA48613 (sequence (XV)) revealed a 400 amino acid long open reading frame sequence with a predicted 26 amino acid long N-terminal signal peptide. The predicted mature protein is 274 amino acids long, with a calculated molecular weight of 41 kD. Potential N-linked glycosylation sites are similar to those in the mouse sequence. The deduced amino acid sequence of DNA48614 (Sequence (XVII)) and comparison to sequence (XV) revealed it to be an alternatively spliced form of DNA 48613, with a 30 amino acid deletion (amino acid positions 127-157, counting from the initiation methionine).

Equivalent Abstract Text (3):

Expression of glial-cell-line-derived neurotrophic factor family receptor alpha-3 (GFRalpha3) mRNA in human tissues was examined by Northern blot analysis. Expression was observed at high levels in the heart, gut, (pancreas, small intestine, colon), thymus, testis and prostate. In in situ hybridization studies using an antisense probe, hybridization was detected in fetal and adult human root ganglia, peripheral nerves (as seen in the body wall and lower limb of the fetus) and mesenteric nerves in the fetus. No expression was observed in the fetal spinal cord or brain.